UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,339	05/17/2002	Paul Alexander Jones	217926USOPCT	6486

22850 7590 09/22/2003

OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER
SPIVACK, PHYLLIS G

ART UNIT	PAPER NUMBER
1614	7

DATE MAILED: 09/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/031,339	Jones et al.
Examiner	**Art Unit**
Phyllis G. Spivack	1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-6 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-6 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

An Information Disclosure Statement filed May 17, 2002, Paper No. 4, is acknowledged and has been reviewed. A publication date is required for each reference.

Claims 1-6 are presented and represent all of the claims under consideration.

Claims 4 and 5 are objected to under 37 C FR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form. The intended use of composition claims confers no patentable weight to the claims. Accordingly, claims 4 and 5 do no further limit the subject matter of claim 3. See In re Hack, 114 USPQ 161.

The disclosure is objected to for the following informality: As an independent claim, claim 3 must show the structure depicted as "compound (1)".

Appropriate correction is required.

Claims 1 and 6 provide for the use of a compound of instant formula I, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 1 and 6 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for

example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 1, 2 and 6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to the treatment or prevention of any acute or chronic cerebral neurodegenerative disease. The specification provides support for protection, specifically for the cortex, in the ET-1 model of stroke by compound I.

Attention is directed to In re Wands, 8 USPQ2d 1400 where the court set forth factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to treatment or prevention of any acute or chronic cerebral neurodegenerative disease.

The relative skill of those in the art is generally that of a Ph.D or M.D.

Each particular cerebral neurodegenerative disease has its own specific characteristics and etiology. The broad recitation "preventing or treating an acute or chronic cerebral neurodegenerative disease" is inclusive of many disorders that presently have no established successful therapies. It would have been reasonable to expect prevention of the many pathologies encompassed in the recitation, comprising administering the compound of formula I, to be unpredictable absent a clear disclosure of the patient population to which prevention is directed.

It is clear the art to which the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy.

The breadth of the claims

The claims are very broad and inclusive of any acute or chronic cerebral neurodegenerative disesase.

The amount of direction or guidance provided and the presence or absence of working examples

The working example is limited to a stroke model wherein protection of the cortex is asserted.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to which particular disease state, other than stroke, may be prevented or treated with a reasonable expectation of success. The skilled artisan would expect the interaction of tacrolimus in the treatment or prevention of a particular cerebral neurodegenerative disease state to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for its administration. The instant specification sets forth no such understanding nor any criteria for extrapolating beyond the protection afforded to the cortex in a stroke model. Beyond the example shown, no direction is provided to treat any other condition beyond stroke. Absent reasonable *a priori* expectations of success for using tacrolimus to treat or prevent a particular cerebral neurodegenerative disease, one skilled in the neurology art would have to test extensively many disease states to discover which effectively responds. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Kelly et al., U.S. Patent 5,648,351.

Kelly teaches the administration of macrolides of formula I for their neuroprotective activity. The compound of the present invention, tacrolimus, is disclosed in column 4, also known as FK506. Pharmaceutical compositions are taught in column 5, lines 25-46. Kelly's teaching is specifically directed to preventing or treating cerebral ischemic disease, such as brain damage caused by ischemia, as a result of cerebral infarction. The acute cerebral diseases are subarachnoid hemorrhage, or intracerebral hemorrhage, cerebral thrombosis and cerebral embolism. Accordingly, Kelly teaches both acute and chronic cerebral neurodegenerative diseases wherein a progressive loss of neurologic functions occurs.

No claim is allowed.

Any inquiry concerning this communication should be directed to Phyllis Spivack at telephone number 703-308-4703.

September 17, 2003

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER